TUFTS CANCER RESEARCH CENTER
OFFICE OF THE DIRECTOR

TUFTS UNIVERSITY
SCHOOL OF MEDICINE

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BOSTON, MASSACHUSETTS 02111

July 30, 1973

Dr. William U. Gardner, Chairman
Scientific Advisory Board
The Council for Tobacco Research
110 East 59th Street
New York, New York 10022

Dear Dr. Gardner:

I am pleased to submit with this letter a grant application entitled "Embryonic Gene Activation in Bronchogenic Cancer".

From the general point of view, it represents an experimental approach to cancer which is based on rather new information which began to appear in the literature since 1965. At first, it was α-fetoprotein which is a fetal gene product recognized in human hepatoma. Then, in 1967, a protein of the fetal gastrointestinal tract was discovered in human gastrointestinal cancers (CEA). Shortly afterward, the Tufts group encountered in lung cancer the Regan isoenzyme which is a placental alkaline phosphatase. Most recently, human chorionic gonadotrophin, another placental protein, has been identified in a variety of non-trophoblastic tumors. The literature now reflects a broadening interest and enthusiasm for the study of embryonic gene products in human cancer and their significance.

Our own experiences with the Regan isoenzyme have prepared us for systematic studies of a number of these carcinoembryonic proteins. These experiences have included the preparation of pure placental alkaline phosphatase, the study of its phenotypic forms, the discovery and application of specific amino acid inhibitors to its quantitation and histochemical demonstration, the development of ultrasensitive immunoenzyme techniques for its detection and, finally, the completion of extensive clinical studies designed to evaluate its usefulness in prognosis and differential diagnosis. These have all been accomplished in four years after the Regan isoenzyme was discovered.

Specifically, with regard to cancer of the lung, we are challenged to find out what results could be harvested from the application of knowledge in the area of embryonic gene activation. We think that the opportunity to examine biochemically, cytologically, and histochemically the bronchial epithelium geographically in relation to a metaplastic, cancer in situ or a frankly neoplastic area is unique and could elicit the type of information which is truly meaningful. We are hopeful that once we have a basic under-

standing of the role of embryonic gene activation, a logical approach to certain fundamental questions relative to lung cancer can be fashioned.

Should your committee look with favor to supporting our plan of research, the study of cancer of the lung would become a major commitment of all the professional, technical and physical resources of the Tufts Cancer Research Center. It would provide a sharply focused goal towards which the cancer cell phenotype group would orient itself. This, in turn, will be bound to stimulate a lot of research interest in specific problems which would be defined as the project moves ahead.

May I point out that the Faculty identified with the Center is competent in the areas of molecular biology, immunology, isoenzymology, somatic cell genetics, immunoviral oncology and chemotherapy. Accordingly, we are confident of the potential of this group to tackle almost any aspect of the contemporary oncology scene if the interest generated from the proposed research warrants it.

In closing, I wish to express the hope that you may find the application of substantial interest to you and your colleagues and also that you may find yourselves able to provide us the financial support we need to do the job.

I send my best personal regards.

Yours sincerely,

Bill Fishman

William H. Fishman, Ph.D.
Director, Cancer Research Center

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